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Specific Risk Factors

THE USE OF TIME-RELATED EPIDEMIOLOGIC DATA ON SMOKING FOR PLANNING CANCER CONTROL PROGRAMS*

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Cancer prevention Cigarette smoking Epidemiology Program planning

INTRODUCTION

Since approximately 30% of all cancers and 90% of lung cancers are attributable to smoking, a major emphasis of the Division of Cancer Prevention and Control of the National Cancer Institute is a reduction in the prevalence of cigarette smoking. The goals are: (1) to develop a program of funded research to test intervention strategies to determine those that are the most effective and durable in preventing the onset and producing the cessation of tobacco use, and (2) to translate that research into wide-spread interventions affecting large numbers of people.

In order to understand the potential long term impact of interventions we have been concerned with identifying the major smoking variables that determine cancer patterns in populations. Time-related factors play a major role. Several time-related factors are central to the design and evaluation of smoking programs: (a) the changing prevalence of smoking both in the aggregate population and in specific subgroups over time, (b) changes in the tar content of cigarettes over time, (c) the effect of the duration of smoking on cancer risk, and (d) the effect of varying lengths of time since cessation on the reduction of risk in ex-smokers. These factors, individually and in combination, produce variations in observed patterns of lung cancer incidence and mortality which are complex and often difficult to interpret.

Topics we explored during the program planning process to be reviewed here are: (i) the nature and adequacy of the major relevant data bases, including past and present smoking prevalence patterns and the rates and risks for smoking-related cancers, (ii) selected analytic issues illustrating how time related considerations may affect the interpretation of smoking control efforts, and (iii) our specifications of the requirements for a model to predict the effects of smoking control programs in future lung cancer rates.

NATURE OF PUBLISHED DATA BASES

Detailed information on two categories of data was needed to support our smoking control planning and evaluation activities. First, information on past and present smoking prevalence was reviewed. In the course of analyzing the content, time coverage, and other characteristics of the available surveys, we participated in the development of a comprehensive inventory of surveys of smoking prevalence [1]. Selected conclusions from this inventory are summarized below. The second class of required data concerns the quantitative relationships between smoking and cancer, derived primarily from several classic prospective epidemiologic studies. Relevant features of both of these categories of data are discussed with reference to characteristics particularly of concern to our planning and evaluation efforts.

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Data on smoking prevalence

There are 17 surveys on national smoking trends sponsored by six agencies (four federal, two voluntary, and one private organization) (Table 1). General analyses of these surveys are provided in publications of the sponsoring agencies, with data from at least half of the surveys available for additional analyses in the form of public use tapes, usually provided several years after the end of the data collection. The surveys vary widely in their content. Key criteria to evaluate the appropriateness of a survey for a particular application are: time frame coverage, age and size of the surveyed population, information on smoking patterns, the definition of smoking behavior used, quantification of the amount smoked, age of smoking initiation and duration of the habit, type and brand of cigarette smoked, and quitting experiences. The extent to which the various surveys meet

Table 1. Overview of smoking surveys

Sponsor: Office on Smoking and Health	
Adult Use of Tobacco Survey (OSH—Adult)	Prevalence and psychosocial data related to smoking behavior of adults (>21 years of age).
Teenage Smoking—National Patterns of Cigarette Smoking (OSH—Teenage)	Data on prevalence, onset, and maintenance of smoking in individuals ages 12–18.
Sponsor: Centers for Disease Control	
State-Based Surveys of Risk Factor Prevalence (CDC—State)	Comparable data by state on eight behavioral risk factors (including smoking).
Sponsor: National Institute on Drug Abuse	
National Household Survey on Drug Abuse (NIDA—NSDA)	Prevalence and trend estimates on the usage of various drugs (including use of cigarettes) among individuals 12 years and older.
National High School Senior Drug Use (NIDA—Seniors)	Data on the prevalence and trends of various forms of drug use (including use of cigarettes) and their relationship with psychosocial variables among high school seniors (17–19 years old).
Sponsor: National Center for Health Statistics	
National Health and Nutrition Examination Survey (NCHS—NHANES)	Cross-sectional data on defined diseases or conditions of ill health, normative data on health-related parameters, and health-related information that can only be obtained by physical examination and clinical/laboratory tests.
National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study (NCHS—NHANES I Follow-up)	Longitudinal data on how factors previously measured in an earlier survey relate to health conditions that have developed since that time.
Hispanic National Health and Nutrition Examination Survey (NCHS—Hispanic HANES)	Provides health and nutrition examination data on persons in families having one or more members of Hispanic origin or descent.
National Health Interview Survey (NCHS—NHIS)	Continuous survey that provides data on the incidence of acute illness and accidental injuries, the prevalence of chronic conditions and impairments, the extent of disability, the utilization of health services, and other health-related topics.
National Natality and Fetal Mortality Survey (NCHS—Natality)	National estimates of births by numerous characteristics, including mother's prenatal health practices.
National Survey of Family Growth (NCHS—Family Growth)	Data on factors influencing trends and differentials in fertility, family planning practices, sources of family planning advice/services, effectiveness and acceptability of family planning methods, and aspects of maternal and child health most directly related to fertility and family planning.
Current Population Survey Smoking Supplement (NCHS—CPS)	Data on smoking behavior for purposes of tracking effects of 1964 Surgeon General's Report on Smoking.
National Survey of Personal Health Practices and Consequences (NCHS—NSPHPC)	Assesses (a) relationship between longevity and seven personal health practices, (b) relationship between health behavior and illness, and (c) role of variables that may intervene between health practices and health consequences.
National Longitudinal Health Survey (NCHS—Long. Health)	Methodological information on the validity of telephone as inquiry mode for obtaining health data.
Sponsor: American Lung Association	
Survey of Public Perception of Smoking Prohibition in Public Places (ALA—Gallup)	Data to assess the public's attitudes toward prohibiting/restricting smoking in public places.
Sponsor: American Cancer Society	
Cancer Prevention Study I and II (ACS—CPS)	Longitudinal data on the role of environmental factors in the etiology of various types of cancer.
Sponsor: Gallup Organization Inc.	
Gallup Omnibus Smoking Audit (Gallup—Smoking Audit)	Data on number of smokers and public perceptions and attitudes toward smoking and its health risks.

Source: Adopted from Massey *et al.* [1].

Table 2. Content and methods of surveys on smoking

Survey	Content area: Definition of smoker	Method of quantifying cigarettes	Age	Age at initiation	Quitting attempts	Brand/type	Sample design	Sample size	Time frames covered/ anticipated
OSH—Adult	>100 cig. + current use	No. smoked	⩾21	Yes	Detailed	Both	National	12,029	1964, 1966, 1970

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Table 2. Content and methods of surveys on smoking

Survey	Content area: Definition of smoker	Method of quantifying cigarettes	Age	Age at initiation	Quitting attempts	Brand/type	Sample design	Sample size	Time frames covered/ anticipated
OSH—Adult	>100 cig. + current use	No. smoked	≥21	Yes	Detailed information	Both	National probability	12,029	1964, 1966, 1970 1975, 1985
OSH—Teenage	>100 cig. + current use	No. smoked	12–18	Yes	Detailed information	Both	Stratified probability	2639–10,000	1968, 1970, 1972 1974, 1979, 1985
CDC—State	>100 cig. + current use	No. smoked	≥18	Yes	Ever attempted?	No	Multistage cluster	22,258	1981, annually thereafter
NIDA—NSDA	1979 only: >100 + past 30 days; Others: smoked within past month	Fixed intervals given	12–17 ≥18	Yes	No	No	National probability	3200–8000	1971, 1972, 1974, 1976, 1977, 1979, 1982, 1985
NIDA—Seniors	Any smoking in past past 30 days	Fixed intervals given	17–19	Yes (grade)	No	No	National 3-stage sampling	16,000	1975, annually thereafter
NCHS —NHANES I & II	>100 + current	No. smoked	I 25 II ≥ 12	Yes	No	No	Multistage clustered probability	21,000	1970–74 (I) 1976–80 (II) 1987–91 (III)
NCHS—NHANES I Follow-up	>100 + current	+ heaviest ever	35–85	Yes	Detailed	Type only	National probability	14,000	1982–1984
NCHS—Hispanic NHANES	>100 + current	+ heaviest ever	≥12	Yes	No	Both	National probability	12,000	1982–1984
NCHS—NHIS	>100 + current	No. smoked	17–19 varies by year	Yes	Detailed (varies by year)	'78–'80 Both	National probability	12,000–75,000	1965, 1966, 1970 1974, 1976, 1977 1978, 1979, 1980 1983, 1985
NCHS—Natality	12 months before delivery	No. smoked	All mothers	No	No	Both	National probability	6400	1963, 1964–1966, 1967–1969, 1972 1980
NCHS—Family Growth	Any during pregnancy	Fixed intervals given	≥15	No	No	No	Multistage area	9797	1982–1983 (III)
NCHS/NCI/OSH—CPS	>100 + current	No. smoked	≥17	Yes	No	Type only	National probability	45,000–75,000	1955, 1966, 1967, 1968
NCHS—NSPHPC	>100 + current	No. smoked	20–64	No	Ever attempted?	No	National probability	2453–3025	1979 (I) 1980 (II)
NCHS—Long. Health	>100 + current	No. smoked	≥18	Yes	Detailed	Both	National probability	9000	1980 (I) 1981 (II)
ALA—Gallup	"Regular smoker"	No. smoked	adults ≥18	No	No	No	National probability	1509	1983
ACS—CPS I and II	>1/day for 1 year	No. smoked + heaviest ever	≥30	No	No	Both	Volunteers	>1 million	1959–1972 (I) 1982 (II) Biannual follow-up
Gallup—Smoking Audit	Any in previous week	No. smoked	≥18	No	Ever attempted?	No	National probability	1500	1977, 1981

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these data needs is given in detail in Table 2. Highlights are summarized below.

Survey target populations vary on the basis of age. Adults are defined as either 18 or older or 20 or older. Two surveys focus on teenagers exclusively, and six of the surveys include both teenagers and adults. The majority of surveys employ national probability samples that range in size from 2000 to 75,000. Personal interviews are used in 8 of the 17, with the remaining using telephone interviews and/or self-administered mail questionnaires. Most of the surveys are cross-sectional, with little data on the behavior of cohorts and longitudinal smoking patterns. A notable exception is the NHANES I Follow-Up Survey. In addition, data on some aspects of cohort smoking behavior can be obtained from some of the longer term observational studies such as Framingham [2] and the VA Normative Study [3].

The intervals between surveys are in general sporadic, with the Health Interview Survey and the National Health and Nutrition Examination Survey providing the most regular coverage. Little systematic survey-based prevalence data exist for periods prior to the mid 1960's. The smoking history data in some of the surveys have been used to construct retrospective profiles of the smoking behavior of various age cohorts. For example, Jeffrey Harris has constructed such patterns for cohorts back to 1900 using smoking histories of respondents to the 1978–80 Health Interview Survey [4].

In general, most of the surveys (10 of 17) define smoking according to the definition established by the National Clearinghouse on Smoking and Health in 1955 (lifetime consumption of 100 or more cigarettes and currently smoking), although comparisons across surveys have sometime been complicated by differences in definitions.

All of the surveys include some information on the number of cigarettes smoked. Nine of the surveys include information on the type and/or brand of cigarettes smoked. In general, information on cessation is rather limited: only eight surveys collect information on quitting experiences, with three of the eight indicating only whether or not the subject had ever attempted to quit. The remaining five collect more detailed information on quitting attempts.

A number of the surveys also collect information on more specialized topics in addition to the more basic questions dealing with prevalence, amount smoked, and cessation attempts described above. Such topics include the use of chewing tobacco and snuff, exposure to passive smoking, smoking in minority populations such as Hispanics, smoking during pregnancy, and attitudes towards regulatory measures to control smoking.

In addition to self-reported smoking behavior, smoking prevalence can also be surmised from cigarette sales figures published by the Department of Agriculture [5] and the Tobacco Institute [6]. Aggregate national and regional trends can be surmised, but no demographically specific information is available. Whereas little reliable survey data exist prior to the 1960's, reliable cigarette consumption data exist from the early nineteen hundreds.

Discrepancies between self-reported consumption and cigarette sales figures have been reported. A comparison of four U.S. surveys from 1964 through 1975 shows a possible trend in underreporting cigarette consumption [7]. A more recent study in New Zealand shows a continued but unchanged degree of underreporting over the period 1976–1981 [8]. An examination of the recent U.S. Health Interview Survey (1980) using Harris' approach [4] and comparing to recent sales data shows that underreporting is still considerable (reported consumption is only 77% of U.S. sales) but is in fact better than that seen in the mid-1970's (Kessler and Brown, unpublished). This approach can easily be extended to compare estimated sales and number of cigarettes smoked back in time. However, these comparisons are limited by recall problems and by the small number of elderly respondents available in most surveys, making estimates of elderly smoking, even in the recent past, quite unstable.

In general, the available survey data on smoking prevalence are adequate for assessing general trends in smoking prevalence on a national level. The samples are representative of the general population and large enough to be reported by age, race, and sex, although up-to-date data on adolescents is scanty in comparison to adults and rapid public availability of survey results is often not possible. For the purposes of planning a strategy of smoking control and projecting its future effects, several additional features are desirable and could be incorporated into the planning of future surveys. First, information on the relative degree of error in self-reported smoking in the various age, race, and sex specific subgroups in national survey samples would provide a useful correction

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factor for cases where cigarette sales data and self-reported consumption do not agree. Further study on how underreporting has changed over time, as suggested by Warner, would be warranted. Second, more longitudinal data on the smoking behavior of large representative cohorts are needed along with the largely cross-sectional data presently available. In addition to documenting changing risk in the population, this information would be useful to describe changing patterns of recidivism, brand switching, changes in numbers of cigarettes smoked, influence of age and changing health status on cessation, etc. Third, although the large surveys presently conducted can be stratified into demographic subgroups, there is little systematic information available on geographically defined populations, e.g. communities. Thus one knows little about the natural history over time of locales exposed to formal and informal anti-smoking influences. Last, and perhaps most important for forecasting purposes, is the lack of detailed and reliable information on the past smoking behavior of older cohorts that are now entering their high-risk period for smoking-induced cancers. This is obviously not correctable for present forecasting exercises, but should be less of a problem in the future because of the national survey efforts of the last 20 years.

Data on smoking and cancer

Many of the conclusions concerning the health effects of smoking are based on eight major prospective (cohort) studies (Table 3) [9]. Most of these studies were initiated in the early and mid-1950's, with the start dates extending from 1951 to 1963. All of the studies were of large numbers of subjects, with the smallest being the British Physicians Study (40,000) and the largest the ACS 25-State Study (840,000). Most of the data are for men, with the ACS 25-State Study the only U.S. study with detailed data on women. Foreign studies with female data are the Swedish Study, British Physicians Study, and Japanese Study. In all of the studies, the assessment of smoking history was by self report, with no validation by biochemical means. The length of followup times varies from about 4 years in the ACS 9-State Study to 16 years in the U.S. Veterans Study and 20 years in the British Physicians Study. The majority of these studies are characterized by almost perfect vital status ascertainment at followup. Most of the studies are not of random population samples but of self-selected groups such as insurance policy holders, veterans of military services, particular occupations, members of unions, and volunteers. Most of them collected data on dose–response relationships, duration of smoking, and time since cessation. Information on pipe and cigar smoking is also available. Because the studies were, for the most part, done in the 1950's, they do not provide any information on cohorts with prolonged exposure to the effects of low tar cigarettes.

Table 3. Prospective studies of lung cancer and smoking

Population	Size	Initiation
British Physicians	34,000 Males 6,194 Females	1951
ACS 9-State Study	188,000 Males	1952
U.S. Veterans	290,000 Males	1954
California Males in 9 Occupations	68,000 Males	1954
Canadian Veterans	78,000 Males	1955
ACS 25-State Study	358,000 Males 483,000 Females	1957
Swedish Study	27,000 Males 28,000 Females	1963
Japanese Study	122,000 Males 143,000 Females	1965

Source: Surgeon General's Report [9].

A large number of case–control studies also exists in addition to the prospective studies, dating from the late 1930's through 1970. A series of reports on 7000 lung cancer patients and 11,000 controls provides much more recent data from cases that were detected from 1976 to 1980 in five European countries. The collaborators have presented results on the change in lung cancer risk after cessation [10] and differentials in risk from filter vs nonfilter cigarettes and from cigarettes of varying tar yields [11].

Examples of important methodologic issues common to all studies of this type include the appropriate classification of smokers, selection bias, and validity of self-reported smoking behavior. These are commented on below.

Appropriate classification of smoker. Ideal categories are never smoker, current smoker, and former smoker. To achieve appropriate distinctions between risk levels, nonsmokers should be separated into former smokers (further classified on the basis of the number of years since quitting) and never smokers. The inclusion of former smokers in the never smoker category can result in overestimates of cancer rates for nonsmokers, and hence underestimates of relative risk.

Selection bias. Since the presence of medical problems often determines the choice to quit, some studies distinguish former smokers who

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quit for medical reasons from those who quit for other reasons. Failure to distinguish those who quit for medical reasons in studies of the effects of cessation on the change in risk status could produce apparently anomalous findings of increased risk in the early years immediately following cessation.

Validity of self-reports. The possibility of bias in recall is always an issue when self-reported behavior is not validated by objective means. Although several reliable biochemical validation methods exist, they were not routinely employed in large-scale epidemiologic studies because of cost and/or were not available when the classical prospective studies were done. Inaccurate recall may occur for a variety of reasons: simple forgetfulness; influence of social desirability, which may cause present smokers to underestimate consumption and former smokers to overestimate consumption; and the influence of cancer patients' knowledge of the diagnosis upon recall.

As discussed previously, large surveys of smoking behavior in the general population in the 1970's suggest that substantial levels of underreporting occurred when the amount reported smoked is compared to the amount sold. The extent of this phenomena in the population at large in this decade is not known. However, smaller studies (200–2000) of the general population in California [12] and of patients attending a clinic in Great Britain [13] have reported "deception rates" of only a few percent when self reports are compared to biochemical indexes of smoking. What is clear, however, is that deception rates are generally quite high (up to 40%) in adults after smoking cessation intervention [14]. In the Multiple Risk Factor Intervention Study, men at high risk of cardiovascular disease received intervention during the 1970's [15]. Initially, 40% of the intervention group reported stopping, with 13% failing biochemical validation, reducing the quit rate to 28%. Discrepancies among the control men were negligible.

The conclusiveness of the smoking–cancer relationship derived from the classical prospective studies is incontrovertible. However, when they are used in planning a smoking control program and projecting its future effects, certain caveats must be observed to avoid misinterpretation. The most notable consideration is that the relative risks that are derived from these studies—all initiated in the 1950's—may not accurately predict the risk to be experienced in the future by today's smoker. Relative risks from the older studies that were uncontrolled for duration of smoking and for changes in the tar level may be inaccurate when applied to forecasting future effects. Also of concern is the lack of data on females. The recency of peak smoking prevalence in this group accounts for the fact that the data from the older studies have provided considerable underestimates of the true current risks. These and other issues will be discussed in more detail in the following section.

SELECTED ANALYTIC ISSUES

In reviewing the determinants of smoking-related cancer trends and the nature of the available data bases, four key time-related issues central to predicting the effects of smoking control efforts were identified: (1) changing prevalence of smoking in the aggregate population and in specific subgroups over time, (2) changes in the tar content of cigarettes over time, (3) the effect of duration of smoking on cancer risk and (4) the effect of varying lengths of time since cessation on reduction of risk in ex-smokers. In the sections below, factors 1 through 3 are treated together in terms of their interactive effects upon trends in relative risks observed over time. Factor 4 is treated separately. As a preamble to the discussion, the assumptions associated with variation in nonsmoker lung cancer rates over time are discussed.

Nonsmoker lung cancer rates

In predicting the effects of smoking cessation and prevention programs upon lung cancer rates, the principal concern is with the expected variation for the preventable proportion of the disease, i.e. the risk attributable to smoking. It is therefore of interest to know the rates for nonsmokers, the variation with age and with other environmental factors, and trends over time.

Estimates of nonsmoker lung cancer rates have been primarily from three of the large prospective studies, the ACS 25-State [16, 17], the U.S. Veterans Study [18, 19], and the British Physicians Study [20], and also from studies of nonsmoking populations such as members of the Mormon Church in California and Utah [21]. There is close agreement of age-adjusted rates for the three prospective studies dating from 1951 to 1960. For males, this rate is about 10–13 per 100,000. In their study of Mormons from 1966 to 1970, Gardner and Lyon obtained similar age-adjusted rates. However, higher

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rates for both the earlier period of 1966–68 and for 1967–75 have been obtained by Enstrom [22].

These high rates do not reflect an actual increase in nonsmoking-related lung cancer but rather a methodological artifact due to inclusion of ex-smokers with never smokers. Age-specific nonsmoker lung cancer rates from the ACS-25 State Study are shown in Table 4. The multistage theory of carcinogenesis [23] suggests that the increasing incidence rates can be approximated by a function of age as follows: rates $= \alpha \cdot \text{age}^B$. This has been done separately for males and females for the ACS data. The strong exponential gradient by age illustrates the importance of this time factor.

Although there is no evidence to contradict the conclusion that lung cancer rates are stable over time in nonsmokers, there are factors that can elevate nonsmoker rates to a degree that is as yet unknown. The effect of these factors is likely to be small in comparison to those for smoking. These factors include occupational exposure, passive smoking, dietary factors, and environmental pollution. Lyon *et al.* have cautioned that the use of relative risks derived from studies in which the comparison groups were influenced by these factors could lead to substantial underestimates of the true risk [24].

Trends in lung cancer and smoking-related relative risks over time

After assessing the baseline rate of lung and other smoking-related cancers, we can assume that excess rates are largely a function of the smoking histories represented in the population. Age, duration of smoking, amount smoked, and type of cigarette are the principal determinants of an individual's risk of developing lung cancer [9, 25, 26]. The first two of these are quite clearly time-related factors, but major changes in all of these factors have characterized the U.S. smoking patterns over most of this century and contribute to the considerable variation in relative risks across the eight major prospective studies [17]. More minor contributions have been from occupational and dietary factors as noted by Lyon *et al.* [16].

Changes in the population prevalence of smoking and concomitant reductions in the tar yield of cigarettes over time have influenced lung cancer patterns and will continue to have dramatic effects. These two exposure characteristics, at least in the United States, cannot be clearly separated from each other. The prevalence of smoking among young men peaked in the years surrounding World War II, while significant changes in the tar yield of cigarettes began to occur in the 1950's. Thus in the country, predicting the direction of lung cancer mortality patterns is difficult because of the temporal overlap of the delayed effects of peak cigarette smoking prevalence with decreases in tar yield of cigarettes [25, 26]. As evidence mounts concerning the relative effects of high vs lower tar cigarettes in the production of lung cancer [11, 27, 28], it may be possible to separate the emerging trends in this country into components due to tar changes and to smoking prevalence.

Table 4. Lung cancer death rates per 100,000 person years for male nonsmokers*

	Period 1: July 1960–June 1964	Period 2: July 1964–June 1968	Period 3: July 1968–June 1972	Function fit to data†
35–39	—	—	—	—
40–44	—	(8.7)	(14.3)	2.4
45–44	(4.0)	(5.1)	—	4.1
50–54	(5.3)	8.8	(8.8)	6.8
55–59	10.5	11.6	8.3	10.8
60–64	17.0	17.3	17.5	16.4
65–69	18.6	29.4	34.3	24.2
70–74	32.3	26.4	19.2	34.6
75–79	32.7	41.5	58.6	48.4
80–84	(47.9)	106.8	51.9	66.3
85–89	61.8	152.7	(69.9)	89.0
Number of deaths	52.0	74.0	69.0	
Age-standardized death rate (1965 Standard)	12.5	18.5	15.8	

*ACS prospective study, Garfinkel (1981).
†Equation fit: $\alpha \cdot \text{age}^B$; $\alpha = 1.79 \times 10^{-5}$, $B = 5$. Estimates by S. Piantadosi and D. Byar.

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A natural experiment is about to mature fully in the U.K. where per capita smoking consumption did not decline sharply until the late 1970's. Tar levels, however, were already greatly reduced by the end of the 1960's. Already, large declines of one-fifth to one-third in age-specific rates of lung cancer among younger males are being observed in the U.K. compared to men of that age 10 years previously [28, 29]. Analyses of these data should allow a population-based estimate of the proportion of excess lung cancer risk that is attributable to the tar content of cigarettes. An additional natural experiment in France will mature somewhat later than the U.K. due to a lag in changes in cigarette composition. Some types of French cigarettes (occupying a nontrivial portion of the market) are air-cured rather than flu-cured. The resulting product is much more like pipe or cigar tobacco for which the lung cancer risk is considerably lower when compared to cigarettes. Again, an analysis should soon give additional clues that are meaningful for both the epidemiologic and public health implications of the smoking–cancer relationship. The recent European data from Lubin *et al.* point to reductions of 40–50% in risk for lifelong users of filter cigarettes as compared to nonfilter users, with the role of tar yield less clearly distinguishable [10, 29].

The effect of duration of smoking on the relative or absolute risk of lung cancer incidence needs to be considered in cancer control projections. However, evidence is sparse regarding the time/duration effects controlled for amount smoked. Doll and Peto [30] explicitly estimated an approximate duration effect while controlling for the amount smoked in the same equation. An analysis of aggregate data in England and Wales by Townsend, using a generalization of this model, produced very similar results [31]. No U.S. data have been used with these models to date, but we have begun to examine the data from the study of U.S. Veterans [18] to confirm these dose and time relationships. Figure 1 shows a plot of the relationship between (approximate) smoking duration and lung cancer mortality, unadjusted for the amount smoked. The linear trends in both age groups show a strong dependence of lung cancer on smoking duration that accumulates gradually as some high polynomial power of years smoked. This is completely consistent with the work by Doll and Peto [30] and Townsend [31] noted above. Points A and B are the lung cancer mortality rates for veterans

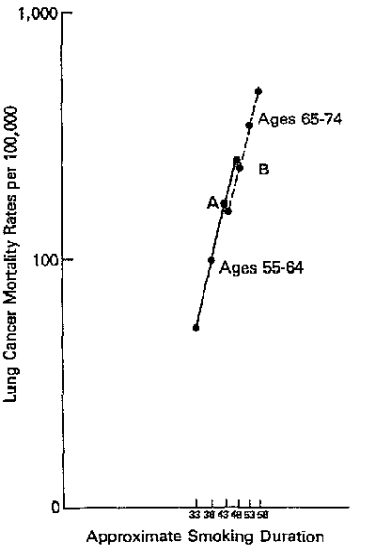

Fig. 1. Lung cancer mortality rates per 100,000 and smoking duration among U.S. male veterans ages 55–64 and 65–74.

who have smoked 43 and 48 years, respectively shown for different age cohorts. Despite an average difference of 10 years in the initiation of smoking, the lung cancer mortality rates are virtually identical for men with the same duration of smoking, showing duration as the key determinant of the lung cancer rates. Knowledge of duration of smoking is therefore crucial for predicting the effect of cessation campaigns on future lung cancer incidence.

We have attempted to calculate very recent estimates of smoking–lung cancer relative risks. Smoking profile data generated from the National Health Interview Survey by Harris [4] were used with U.S. lung cancer mortality data and nonsmoker data from the ACS prospective study to estimate the relative risks of lung cancer for smokers by age–sex group in 1975 (Table 5). The methods are explained in detail in Appendix A. The trend in relative risks is a function of age and cohort exposure effects and produces the somewhat unusual pattern in the table. Consistently lower risks of smoking among females, as expected, are due to the duration of smoking among similar age cohorts and, perhaps to a lesser degree, to differences in consumption of lower tar cigarette brands [27].

There are reasons to be suspect of the high relative risks for some age groups, the severe decline in relative risks among the elderly, and the flatness of the curve for males aged 50–75.

Table 5. Esti
risks of

Age
30–34
35–39
40–44
45–49
50–54
55–59
60–64
65–69
70–74
75–79
80–84
85+

*Data from
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Table 5. Estimates of age–sex specific relative risks of smoking and lung cancer*

Age	Males	Females
30–34	3.9	4.5
35–39	11.9	9.4
40–44	18.1	16.9
45–49	26.5	22.2
50–54	33.7	24.6
55–59	37.9	26.9
60–64	37.0	25.3
65–69	47.9	34.3
70–74	39.1	23.6
75–79	42.4	26.5
80–84	27.4	12.2
85+	13.0	2.9

*Data from Harris [4] (smoking prevalence); SEER (1973–1977). Curve fit to data from Garfinkel [17].

Despite the fact that few studies have shown such high relative risks, risks approaching 40 have been shown by analysis of aggregate U.K. data by Stevens and Moolgavkar [32], and we believe that the rates in our table are consistent with the U.K. data. The flatness of risks between ages 50 and 75 is more difficult to explain and is likely a function of complex cohort and period factors. However, concerning the decline of risk among the elderly, relative risks and absolute incidence rates for a population examined at older ages are partially a function of the mortality increases due to smoking that have differentially affected each distinct birth cohort. If a more cancer-susceptible group among the smokers in the population exists, then the relative risk of those remaining after the susceptible begin to die will decline. The general issue of importance is that these relative risks not only change over age but also may be changing over time, as suggested by these recent high estimates in contrast to estimates from previous studies.

Cancer risk after smoking cessation

Our understanding of trends in cancer incidence and smoking-related relative risks also depends upon data that accurately predict cancer risk after smoking cessation. The major issues of concern are how fast relative (and absolute) risks of cancer change after smoking cessation; the magnitude of the change; and whether the rate and amount of change are known to vary by demographic or other relevant characteristics.

The large prospective epidemiologic studies provide the best evidence concerning change in risk after cessation of smoking. The data in Table 6, reproduced from the 1982 Surgeon General's Report, are relevant to lung cancer only and illustrate the problem of understanding this time factor. The U.S. and British studies show little decline in lung cancer mortality relative to nonsmokers until at least 5 years after quitting, with the ACS showing an earlier decline. However, and even more striking, is that after 10 years, the relative mortality among the ACS cohort was virtually 1 (or less) in contrast to the other studies. A number of factors related to study design or population differences likely underlie these differences. An alternative to using one estimate from these data to describe the temporal relationship between quitting and cancer development may be to consider the general rule suggested by Doll and Peto [30]. In this model, the lung cancer rate among smokers is assumed to be composed of the background (nonsmoker) rate, which depends on age, and the excess rate, which depends upon duration of exposure. After smoking ceases, the absolute excess risk of lung cancer freezes, and the risk relative to continuing smokers decreases over time.

Additional opportunities are now emerging for analysis of those questions. For example, a recent large European case–control study may produce new relative risk estimates, especially

Table 6. Lung cancer mortality ratios in ex-cigarette smokers, by number of years stopped smoking

Study	Years stopped smoking	Mortality ratio	
British Physicians	1–4	16.0	
	5–9	5.9	
	10–14	5.3	
	15+	2.0	
	Current smokers	14.0	
U.S. Veterans*	1–4	18.83	
	5–9	7.73	
	10–14	4.71	
	15–19	4.81	
	20+	2.10	
	Current smokers	11.28	
Japanese Males	1–4	4.65	
	5–9	2.50	
	10+	1.35	
	Current smokers	3.76	
		Number of cigarettes smoked per day	
		1–19	20+
ACS 25-State Study (males 50–69)	<1	7.20	29.13
	1–4	4.60	12.00
	5–9	1.00	7.20
	10+	0.40	1.06
	Current smokers	6.47	13.67

*Includes data only for ex-cigarette smokers who stopped for other than physicians' orders.

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in terms of cessation behavior [10]. Since this data base includes both smoking amount and duration, this data may be useful to understand better or even confirm several hypotheses concerning recent lung cancer trends.

Models of carcinogenesis, particularly the multistage model, applied to population-based data over time may give a number of clues that will assist us in the cancer control field [33]. This approach to analyzing potential preventive efforts has been suggested by Day and Brown [33] and is further elaborated in this journal issue [34]. An important example of such an analysis involves the rapid increase in lung cancer among women. The rapid increase of smoking prevalence among women beginning in the second half of this century is only now becoming visible as a rapid increase in female lung cancer rates. Can this be slowed down and by how much? Brown and Chu [34] suggest that the predominant influence of cigarette smoke in the development of cancer is its effect on tumor promotion, with an important but relatively smaller effect on the tumor initiation phase. This suggests that cessation campaigns directed at long-term and/or heavy smokers could play an important role in the reduction of cancer incidence. Quantification of the effect of cigarette smoking on the stage of cancer development is a key element that should allow us to estimate the ability of an anti-smoking effort to contain the expected continuing rapid increase in lung cancer among females.

REQUIREMENTS FOR A FORECASTING MODEL

The public health planner can allocate resources to only a few of many potential anti-smoking activities and must maximize the effectiveness of resources allocation decisions using systematic rules. Therefore, a comprehensive mathematical model that addresses the effects of the time-related factors on population aggregates discussed above would be of considerable value. Ideally, such a model would use recent historical data to enable us to understand the reasons for present trends in smoking-related cancers. In addition, health planning would be greatly assisted if these models could provide projections of the incidence and mortality of smoking-related cancers for the near future. Indeed, for smoking prevention efforts aimed at the adolescent period, the ability to include a horizon of at least 50 years is desirable.

A model to estimate the impact that national cessation and prevention efforts will have on smoking-related cancers, including the capability for separate analysis of high-risk target populations and the estimation of cost-benefit tradeoffs, would be an invaluable forecasting tool for public health planners. Such a population forecasting model for lung cancer has been developed by Hakulinen and Pukkala [35], which has several elements of the modeling process that are particularly relevant to planners. The Finish model is described briefly in Ref. [35], and several simulation runs are presented showing possible effects of dramatic changes in smoking on future lung cancer incidence. The model we envision would perform much as that of Hakulinen and Pukkala. Here we amplify elements of the model and describe specifications and assumptions for an ideal model, with reference to ongoing projects attempting to construct algorithms responsive to these needs.

A popular model with some of the key features discussed in this paper is the technique of age–period–cohort modeling (APC). This model has been used specifically with lung cancer data by several investigators, including Osmond and Gardner [36], Day and Charnay [37], Kupper *et al.* [38], and Stevens and Moolgavkar [39]. In general, these investigators conclude that the trends in the U.K. and elsewhere tend to exhibit both period and, particularly, cohort effects, and these are driven by the smoking behavior of the population over time. By themselves, these models do not represent forecasting efforts, rather they have been used to fit historical data and discuss functions of there empirical exercises, such as estimation of relative risks.

However, projections of the estimated period and cohort effects (along with assumptions about any future changes in age effects) allow forecasts of cancer rates by these APC models. The difficulties in using these models directly for projections are twofold. First, identifiability and estimation of the parameters is a methodological problem in APC models in general [38], but some researchers have suggested approaches that may be useful with U.S. data [37]. The other major difficulty is the need to tie population smoking data to the parameter projections of this type of model. Following Hakulinen and Pukkala [35], the parameters

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from APC models can be used as the foundation of a simulation model, which then estimates future incidence rates as a function of smoking projections tied to these parameter projections. However, this process is complicated by the complex interrelationships of the time factors discussed previously in this paper.

Specification of smoking control program parameters

In addition to accurate estimates of trends in relative risks of current and former smokers as discussed above, the cancer control planner must estimate the potential effects that anti-smoking efforts may have on the target populations. Smoking cessation and prevention programs may produce a wide range of effects. Initiation of regular smoking by young people can be completely prevented, or it can be delayed by a given number of years. Individuals may stop smoking completely, or they may reduce the number of cigarettes smoked, or they may change to a cigarette brand yielding less tar. Changes in smoking habits may be long lasting, or a return to former smoking habits may occur once or many times over the course of an individual's smoking history.

The variety and possible combinations of program outcomes requires that the cancer control researcher carefully analyze any interventions to be used as an input variable for exercises to model future lung cancer rates.

Relevant questions to be asked include: What are the short- and long-term success rates? How well have they been verified by biochemical assessment of smoking status? Have the results been replicated by other investigators in other settings? Can the success rates be achieved in all segments of the target population, or are the effects limited to particular subgroups? Is the intervention generalizable beyond self-selected volunteers? Is the intervention practical and sufficiently cost-effective to achieve widescale implementation of the program? Is cost per quitter data readily separable into costs associated with the research evaluation component vs costs for implementation in a non-research setting? The extent of information on this list of ideal parameters is variable at present, but increasing as funding agencies place greater emphasis upon large scale randomized trials with strong process evaluation components, especially community-based intervention strategies.

Data requirements and assumptions for modeling the impact of smoking control programs

To estimate the relative impact of various smoking control strategies on lung cancer incidence, we have been part of an effort aimed at the development of a model that projects the effects of intervention programs on cancer mortality [40, 41]. The importance of time factors that relate smoking to cancer is illustrated by presenting the basic structure and goals of the modeling effort. Details of methodology and results are presented by Eddy [40] and Levin [41] elsewhere.

The model requires baseline population data and incidence or prevalence data and allows specification of a hypothetical smoking control program. The following input data are required: (1) the age- and sex-specific target population of the intervention; (2) the proportion of the target population who smoke; (3) the proportion of the target population in whom the intervention is successful; (4) the relative risk of cancer mortality among smokers compared to nonsmokers, taking into account the amount smoked, duration, age started, etc.; (5) the degree to which this risk declines over time following cessation; (6) a delay or startup time until the intervention begins to have an effect; (7) whether the intervention program will stop at some point in the future; (8) whether such a stoppage diminishes the effect among those who have been affected; and (9) whether each new age cohort entering the age-group target population is included in the intervention program.

Application of this model requires that the following assumptions be made.

(i) The available estimates of relative risks for lung cancer for nonsmokers, future smokers, and future ex-smokers are appropriate. The issues involved in using data from the classical prospective studies as well as the problems in estimating risks for more recent cohorts have been discussed.

(ii) Estimates of the effects of hypothetical programs based on the experience of recent experiments and demonstrations are appropriate. We have alluded to the complexities of cessation–recidivism cycles and the considerations involved in generalization of the effects of experimental programs to widescale applications.

(iii) Risk factors for lung cancer mortality other than smoking will remain constant in the future.

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(iv) Changes in competing causes of death will not influence projections.

(v) Synergistic interactions of smoking with other cancer risk factors do not occur to any great extent.

(vi) Cancer treatment effectiveness will remain constant in the future.

(vii) Presently available demographic projections for the future are adequate.

These assumptions require continued work to refine methodology and utilize existing data bases appropriately. By listing the key data requirements and assumptions, one may begin to consider the effect of changing one or more of them and building such changes into the model. The questions raised here contribute to setting a research agenda for epidemiologists, statisticians and health planners to produce a comprehensive and practical model to plan and evaluate the large scale anti-smoking efforts required to achieve national disease prevention goals.

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APPENDIX A

Calculation of Age-Specific Relative Risk of Smoking on Lung Cancer

Data available included age–sex specific mortality rates of lung cancer for the U.S. population, age–sex specific lung cancer mortality rates for nonsmokers from the ACS prospective study published by Garfinkel [17], and age–sex specific smoking histories constructed by Harris [4] using the 1980 Health Interview Survey. To smooth out irregularities in the nonsmokers' mortality rates, a polynomial of degree five (on age) was estimated to fit the data, and these estimates rather than the raw data were used (Piantadosi and Byar, personal communication).

Definitions

RR = relative risk
INC = incidence rates
MORT = mortality rates
T = total population
E = exposed (smoking population)
$\bar{E}$ = current nonsmokers
$P(\ )$ = proportion of population exposed or unexposed

$$\mathrm{RR} \doteq \frac{\mathrm{INC}\,E}{\mathrm{INC}\,\bar{E}} \doteq \frac{\mathrm{MORT}\,E}{\mathrm{MORT}\,\bar{E}} \quad (\doteq \text{approx. equal to}) \tag{1}$$

$$\mathrm{MORT}_T = \mathrm{MORT}_E \cdot P_E + \mathrm{MORT}_{\bar{E}}(1 - P_E). \tag{2}$$

[For each age group substituting (1) into (2) yields:]

$$\mathrm{RR} \doteq \frac{\mathrm{MORT}_T - \mathrm{MORT}_{\bar{E}}(1 - P_E)}{\mathrm{MORT}_{\bar{E}} \cdot P_E}$$

$$\doteq \frac{\mathrm{MORT}_T - \mathrm{MORT}_{\bar{E}}(1 - P_E)}{\mathrm{INC}_{\bar{E}} \cdot P_E}. \tag{3}$$

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